

## Spatial Distribution of the Nonlinearity of the BOLD Response

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### Purpose:

To investigate the spatial variation in the nonlinearity of the BOLD fMRI response.

### Introduction:

A central issue in fMRI is the characterization of underlying neuronal activity from the hemodynamic response. Many current methods for fMRI analysis and the relation of observed signal changes to neuronal activity involve the assumption of a linear system. Recent studies have demonstrated that the fMRI BOLD response has some nonlinear characteristics when looking at averaged signal responses (1-3). The focus of this study is to characterize the spatial heterogeneity of the nonlinearity of the hemodynamic response, and to determine whether this pattern is correlated with other measures such as the magnitude or latency of the response.

The nonlinearity of the BOLD signal,  $s(t)$ , is modeled as an additional multiplicative factor,  $f(SD)$ , varying with the stimulus duration but constant across time, affecting the amplitude of the ideal response,  $a(t)$ ,

$$s(t) = [a(t)]f(SD) + \text{baseline} + \text{noise}$$

The goal in this study is to determine the nonlinearity,  $f(SD)$ , for each voxel and derive from this a measure of nonlinearity that can be mapped across space.

### Methods:

A series of echo planar images of the visual cortex was acquired on a GE Signa 1.5T scanner. (TR/TE=1000ms/40ms, 24cm FOV, 7mm sl.thick, 64x64) Visual stimulation was performed using a flashing checkerboard pattern at 4 different stimulus durations – 250 ms, 500 ms, 1000 ms, and 2000 ms – and an inter-stimulus interval of 14 s. Images were also acquired in a blocked trial paradigm, alternating 20 s periods of stimulation with 20 s periods of rest.

An ideal response function (based on a linear model) was generated for each stimulus duration by convolving the stimulus timing with a gamma variate function (4). The amplitude of the response was determined by fitting the function for the appropriate stimulus duration to the each pixel's response time course. This function was allowed to shift in time by up to 4 seconds to account for variations in response latency. To study the spatial variation of the nonlinearity,  $f(SD)$ , without the influence of underlying spatial variation in the amplitude of the linear aspect of the functional response,  $a$ , the amplitude of the fit was normalized by amplitude of the fit to the blocked trial response. This ratio was then plotted as a function of the stimulus duration (see Fig. 1). For a linear system, this ratio would be constant across stimulus durations. The nonlinearity was additionally measured by computing the area of the averaged hemodynamic response divided by the stimulus duration. These curves of normalized amplitude (or area) vs. stimulus duration were reduced to a single measure of nonlinearity by computing the area under this curve. This measure was used to create a spatial map of the nonlinearity.

### Results:

The amplitude of the BOLD response showed a nonlinear behavior with larger amplitudes for shorter stimulus durations than expected from a linear model. A similar result was found for the area of the averaged response. A range of nonlinearities were observed across space (see Fig. 2). These nonlinearities were not significantly correlated with either the magnitude or the latency of the activation response.

### Discussion:

The nonlinearity of the BOLD response results from either a nonlinearity in the neuronal activity or a nonlinearity in the hemodynamics. A more complete understanding of the origins of this nonlinearity is currently being obtained by the studying the correlation of the nonlinearity with other hemodynamic parameters such as regional cerebral blood flow and cerebral blood volume. Understanding the origin of this nonlinearity is crucial both in determining the relationship between the MR signal and the underlying neuronal activity, and in improving the analyses of fMRI responses.

### References:

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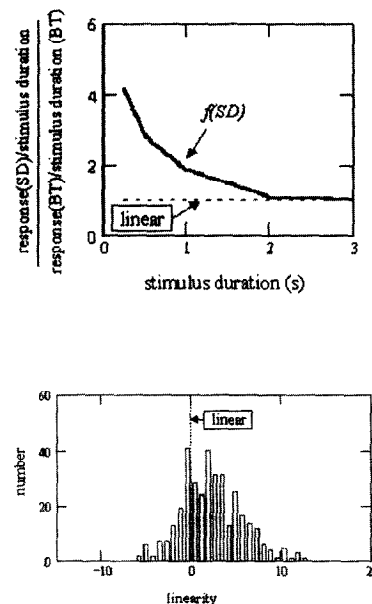


Figure 2: Histogram of the measures of nonlinearity for pixels in the visual cortex.